IBUPROFEN NARCOTIC COMPOSITION AND METHOD FOR MAKING SAME

BACKGROUND OF THE INVENTION

[0001] **Field of the Invention**

[0002] The present invention relates to pharmaceutical compositions and, more specifically to a pharmaceutical composition of ibuprofen and a narcotic analgesic.

[0003] **Description of the Prior Art**

[0004] Ibuprofen is a non-steroidal anti-inflammatory agent commonly known to the pharmaceutical art. Many compositions of ibuprofen show poor tablet compression, poor stability and poor disintegration characteristics.

[0005] Ibuprofen tablets made from wet granulation methods may experience degraded dissolution over time. This may be due to sintering. One method used to reduce sintering is to increase the amount of excipients used in the compositions in order to isolate the ibuprofen particles. However, by increasing the concentration of excipients, problems arise in formulating high dose ibuprofen tablets because the tablets may become too large.

[0006] Solid dosage forms of non-steroidal anti-inflammatory agents in combination with narcotic analgesics are known and have been described as providing a synergistic therapeutic effect for the relief of pain. For example, diclofenac sodium and codeine phosphate tablets are made by mixing the diclofenac sodium and codeine with dicalcium phosphate, corn starch and colloidal silica. Another formulation is spray granulated with a solution of hydroxypropyl cellulose in deionized water. The dried granulation is mixed with carboxymethyl starch, colloidal silica and magnesium stearate. The resulting blend is compressed into tablets and film coated. One formulation for the treatment of pain uses a combination of ibuprofen and hydrocodone bitartrate.

[0007] In a wet granulation method for making various strength ibuprofen and codeine phosphate tablets, the ibuprofen is mixed with microcrystalline cellulose, calcium carboxymethylcellulose and fumed silica. This combination of material may be granulated using a solution of polyvinylpyrrolidone in isopropyl alcohol. The granules are sized, dried and blended with excipients such as calcium carboxymethylcellulose, fumed silica, stearic acid, and sodium metabisulphite.

[0008] Wet granulation of pharmaceuticals may be a relatively time consuming and complicated process. Therefore, wet granulated pharmaceuticals may be considered not to be relatively easy to manufacture.

[0009] Therefore, there is a need for a composition containing ibuprofen and a narcotic analgesic that is relatively easy to manufacture.

SUMMARY OF THE INVENTION

[0010] The disadvantages of the prior art are overcome by the present invention which, in one aspect, is a pharmaceutical composition in a plurality of units (such as tablets or capsules) that includes ibuprofen, in a concentration of between 10% and 84%, by weight, of each of the plurality of units, and a narcotic analgesic, of which each of the plurality of units includes between 1 mg to 60 mg of the narcotic analgesic. Other ingredients include: a disintegrant, in a concentration of between 0.25% to15% by weight of each of the plurality of units; a filler, in a concentration of between 2% to 90% by weight of each of the plurality of units; and a binder, in a concentration of between 0.25% to 20% by weight of each of the plurality of units. At least the ibuprofen and the narcotic analgesic are granulated in a dry compaction process.

[0011] In another aspect, the invention is a method of making a pharmaceutical composition. Ibuprofen, in a concentration of between 10% and 84%, a narcotic analgesic and at least one excipient are mixed in a dry powder phase. The ibuprofen, the narcotic analgesic and the at least

one excipient are compacted to form a substantially dry compact material, also referred to as a compact. The dry compact material is milled, or otherwise sized, to form a plurality of dry granules. The dry granules are compressed to form a plurality of tablets.

[0012] These and other aspects of the invention will become apparent from the following description of the preferred embodiments taken in conjunction with the following drawings. As would be obvious to one skilled in the art, many variations and modifications of the invention may be effected without departing from the spirit and scope of the novel concepts of the disclosure.

BRIEF DESCRIPTION OF THE FIGURES OF THE DRAWINGS

[0013] **FIG. 1** is a block diagram showing a process for making a pharmaceutical composition.

[0014] **FIG. 2** is a table showing several compositions according to the invention.

DETAILED DESCRIPTION OF THE INVENTION

[0015] A preferred embodiment of the invention is now described in detail. Referring to the drawings, like numbers indicate like parts throughout the views. As used in the description herein and throughout the claims, the following terms take the meanings explicitly associated herein, unless the context clearly dictates otherwise: the meaning of "a," "an," and "the" includes plural reference, the meaning of "in" includes "in" and "on."

[0016] In one embodiment, as shown in FIG. 1, the invention is a process **100** for making a pharmaceutical composition of ibuprofen and a narcotic analgesic, such as hydrocodone bitartrate. In a powder phase, the active ingredients **102** are added to inactive excipients **104** and are mixed in a blender **106** to form a powdered combination **108**. The powdered combination **108** is delivered to a dry compactor **110** where it is forced through a pair of compaction rollers

111 to form a plurality of compact materials **112**. The compact materials **112** are milled into a plurality of granules **116** with a mill **114**. The resulting granules **116** are screened **118**. The screened granules **119** may be combined with extra-granular excipients **120** and mixed therewith in a blender **122** for form a combination **124** of granules and extra-granular excipients. The combination **124** is then delivered to a tablet press **130** which compresses the combination into a plurality of tablets **132**. Alternately, capsule shells may be filled with the combination **124** to form a plurality of capsules **134**.

[0017] If extra-granular excipients are not required, the screened granules **119** are delivered directly to the tablet press **130**. Also, the ibuprofen may be granulated, as described above, with the hydrocodone bitartrate, or other narcotic analgesic being added extra-granularly.

[0018] The composition would include the following active ingredients: ibuprofen in a concentration of between 10% and 84%, by weight, of each of the plurality of tablets; and a narcotic analgesic, of which each of the plurality of tablets includes between 1 mg to 60 mg of the narcotic analgesic, such as hydrocodone bitartrate. The excipients may include: a disintegrant, such as croscarmellose sodium, in a concentration of between 0.25% to15%, by weight, of each of the plurality of tablets; a filler, such as lactose and/or a filler/binder such as microcrystalline cellulose and lactose, in a concentration of between 2% to 90%, by weight, of each of the plurality of tablets; and a binder, such as pregelatinized starch, in a concentration of between 0.25% to 20%, by weight, of each of the plurality of tablets. A lubricant, such as magnesium stearate, in a concentration of about 0.59% by weight of each of the plurality of tablets may also be added. At least the ibuprofen and the narcotic analgesic are granulated in a dry compaction process.

[0019] Some illustrative excipients that may be used with the composition of the invention include the following: disintegrants (such as croscarmellose sodium, crospovidone, sodium starch glycolate, pregelatinized starch and starch), fillers and/or filler-binders (such as microcrystalline cellulose, cellulose, and lactose), binders (such as pregelatinized starch and

povidone), and lubricants (such as magnesium stearate, sodium stearyl fumarate and stearic acid). As would be known to those of skill in the art, other excipients may also be employed.

[0020] The dry granulation process according to the invention has utility in that it offers the advantage of improved content uniformity of the composition. This feature is important with low-dosage pharmaceuticals, such as hydrocodone bitartrate. Another advantage of the invention is that it employs a relatively simple process requiring relatively few excipients.

[0021] Several illustrative compositions according to the invention are shown in a table **200** in **FIG. 2**. These compositions include both tablet formulations and capsule formulations.

[0022] The above described embodiments are given as illustrative examples only. It will be readily appreciated that many deviations may be made from the specific embodiments disclosed in this specification without departing from the invention. Accordingly, the scope of the invention is to be determined by the claims below rather than being limited to the specifically described embodiments above.